Amendments

In the Claims

Please amend the claims as follows:

1. (Amended) A transdermal system for the delivery of clonidine consisting of a clonidine-containing pressure-sensitive acrylate-based contact adhesive layer consisting of a copolymer consisting of the monomers 2-ethylhexyl acrylate and vinyl acetate; a covering and, on a side opposite from the covering, a removable support that temporarily covers the contact adhesive layer.

25. (Amended) The transdermal system of claim 19 wherein the contact adhesive layer has a dry weight per unit area of from 20 g/m^2 to 150 g/m^2

26. (Amended) The transdermal system of claim 25 wherein the contact adhesive layer has a dry weight per unit area of from 50 g/m^2 to 120 g/m^2.

Remarks

I. Status of the Claims

Claims 1 and 16-29 are pending in the instant case and stand variously rejected under 35 U.S.C. §112 first and second paragraphs, 35 U.S.C. §102(e), and 35 U.S.C. §103(a). Claims 1, 25 and 26 have been amended herein and a marked up version of the amendments is presented as Appendix A entitled "MARKED UP VERSION OF AMENDMENTS MADE HEREIN". Applicants believe the response and amendments presented herein overcome these rejections and place the instant case in condition for allowance and an indication of such favorable action is solicited from the Examiner.

II. Rejection of Claim 18 under 35 U.S.C. §112, first paragraph is overcome and should be withdrawn

Claim 18 was rejected under 35 U.S.C. §112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed. According to the

Examiner, "...the specification does [not] include description of filler, skin protective substances and the tackifiers in a manner to allow on skilled in the art to practice the invention without undue experimentation." Applicants respectfully traverse.

The present application is directed to a transdermal system for the delivery of clonidine consisting of a clonidine-containing contact adhesive layer consisting of a 2-ethylhexyl acrylate/vinyl acetate copolymer. Such a transdermal delivery system also is contemplated to include fillers, skin-protective substances, and tackifiers (*i.e.*, subject matter of claim 18). The instant specification particularly contemplates the use of fillers, skin-protective substances, and tackifiers *e.g.*, at page lines 9-11 and page 6 lines 9-14.

It is a well known tenet of the law that a specification disclosure need not teach, and preferably ***should omit***, what is well known to those of skill in the art. *In re Buchner*, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). As long as the specification contains at least one method of making and using the claimed invention that bears a reasonable correlation to the entire scope of the claimed invention, then the enablement requirement under 35 U.S.C. §112 is satisfied. *In re Fisher*, 166 USPQ 18, 24 (CCPA, 1970); MPEP 2164.01(b).

At the time the instant invention was filed, those of skill in the art of preparing transdermal delivery devices were well aware of how to produce such devices to include fillers, skin-protective substances, and tackifiers. For example, attached herewith is pages from the United States Pharmacopeia, The National Formulary, which evidences that those of skill in the art were able to produce pharmaceutical formulations that comprise fillers at the time the application was filed (see page 1943, first column, last paragraph; Appendix B). Tackifiers are merely compounds which "make an adhesive stickier" (see attached definition from Hawley's Condensed Chemical Dictionary, 12th Edition, Lewis, Ed., Van Nostrand Reinhold, publ., 1993 attached as Appendix C; see also U.S. Patent 5,962,011 col 7, lines 54-63, attached as Appendix D). U.S. Patent 5,820,878 (Appendix E) which is generally directed to a percutaneously absorbable patch, specifically states that tackifiers and fillers are "conventional additives". See col 3, lines 18-35 where it is stated that:

"...patch of this invention may contain conventional additives in addition to the above essential ingredients. Specific examples of the conventional additives are... tackifiers,... fillers, such as zinc calcium carbonate, titanium dioxide, and silica. They may be added in a suitable amount."

Clearly, methods and compositions that constitute fillers and tackifiers were well known to those of skill in the art of preparing transdermal delivery devices at the time the instant application was filed. Similarly, the idea of using skin protective substances in pharmaceutical compositions also was well known to those of skill in the art, see for example U.S. Patent 5,284,833 col. 8, lines 16-25 (Appendix F; see also U.S. Patent 6,217,890 Appendix G discussed further below). Given that the above teachings are exemplary of what was known to those of skill in the art at the time the application was filed, Applicants submit that the present invention which specifically contemplates the use of fillers, skin-protective substances, and tackifiers is fully enabled in accordance with 35 U.S.C. §112, first paragraph. Applicants request that the rejection be withdrawn and claim 18 be reconsidered for allowance.

III. Rejections of the Claims Under 35 U.S.C. §112, Second Paragraph Are Overcome and Should Be Withdrawn

Claims 18, 25 and 26 were rejected under rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Applicants traverse the rejection.

Claim 18 was rejected as confusing for reciting the term "skin protective substance". The term skin protectant is one that is well known to those of skill in the art. See for example, U.S. Patent 6,217,890 column 15, lines 32-44 (Appendix G) which defines skin protectant as:

"Skin protectants are a drug product which protects injured or exposed skin or mucous membrane surface from harmful or annoying stimuli. Suitable active ingredients, in addition to those mentioned above as suitable emollients, which can be incorporated into the lotion formulation include, but are not limited to, alantoin and its derivatives, aluminum hydroxide gel, calamine, cocoa butter, dimethicone, cod liver oil, glycerin, kaolin and its derivatives, lanolin and its derivatives, mineral oil, shark liver oil, talc, topical starch, zinc acetate, zinc carbonate, and zinc oxide and the like, and mixtures thereof."

Clearly, one of skill in the art of producing transdermal devices viewing claim 18, in light of the specification would understand what is intended by skin protective substances, without requiring an enumeration of each such substance. In light of this response, Applicants submit that claim 18 is sufficiently clear and request that the rejection be withdrawn.

Claim 25 was rejected for lack of antecedent basis for the term "dry". Claims 25 has been reworded so as to recite that the contact adhesive layer has a dry weight per unit area of from 20 g/m^2 to 150 g/m^2. Similarly, claim 26 has been amended to recite that the contact adhesive layer has a dry weight per unit area of from 50 g/m^2 to 120 g/m^2. Applicants believe the amendments to claims 25 and 26 overcome the rejections based on 35 U.S.C. §112, second paragraph.

Applicants believe the amendments and responses presented above remove the grounds for rejection of the claims based on 35 U.S.C. §112, second paragraph. Applicants request withdrawal of the rejection and reconsideration of the application in light of this response.

IV. The Rejections Under 35 U.S.C. 102(e) Are Overcome and Should Be Withdrawn.

Claim 1, 18-20, 22, 23, 25 and 29 were rejected under 35 U.S.C. §102(e) as allegedly being anticipated by U.S. Patent 5,965,155 (the '155 patent). Applicants traverse the rejection.

According to the Examiner the '155 patent discloses a transdermal patch for the treatment of migraine, which patch comprises a contact adhesive layer comprising clonidine in base comprising copolymer of 2-ethylhexyl acrylate and vinyl acetate. According to the examiner the adhesive layer further comprises filler, tackifier and plasticizer, and the patch comprises an impermeable backing and a protective layer of siliconized which is removed prior to use. According to the examiner the structure is inherently multilayered and the adhesive layer has a per unit area of 125 mg/m^2. Applicants respectfully disagree with the Examiner's characterization of the '155 patent.

In the first instance, the '155 patent is directed to a disclosure of a patch of penetetrazole ***not*** clonidine. The only mention of clonidine is at column 1, line 54 where it is listed among a laundry list of agents that are listed to demonstrate that "...there is no single remedy for the prophylactic treatment of all forms of migraine..." There is absolutely no mention of a transdermal delivery method of clonidine anywhere in the '155 patent. Moreover, a review of the '155 patent reveals that the contact adhesives disclosed therein do not consist only of the monomers 2-ethylhexyl acrylate and vinyl acetate. For example, the '155 patent at column 3 lines 58-62 provides that:

> "Preferred acrylate-based polymers are self-crosslinking acrylate copolymers of 2-ethylhexyl acrylate, vinyl acetate and acrylic acid with titanium chelate ester; in the case of non-self-crosslinking acrylate polymers titanium chelate ester is not included."

As such, the '155 does not provide a disclosure of a contact adhesive which consists only of the monomers of 2 ethylhexyl acrylate and vinyl acetate. The present invention is based on the "...surprising finding that a pressure sensitive acrylate-based contact adhesive which consists exclusively of the monomers of 2-ethlyhexyl acrylate and vinyl acetate..." and claim 1 is directed to:

> A transdermal system for the delivery of clonidine consisting of a clonidine-containing pressure-sensitive acrylate-based contact adhesive layer consisting of a copolymer consisting of the monomers 2-ethylhexyl acrylate and vinyl acetate; a covering and, on a side opposite from the covering, a removable support that temporarily covers the contact adhesive layer.

It is a fundamental tenet of the law that anticipation of a claim requires that the reference teach every element of the claim. M.P.E.P. §2131. Thus, "a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Because the '155 does not disclose a patch consisting of a clonidine-containing pressure-sensitive acrylate-based contact adhesive layer consisting of a copolymer only of monomers of 2 ethylehexyl acrylate and vinyl acetate, it cannot anticipate claim 1 of the instant invention. Claims 18-20, 22, 23, 25 and 29 all ultimately depend from claim 1 and

therefore incorporate all the limitations of claim 1. As such, Applicants respectfully submit that all of claims 18-20, 22, 23, 25 and 29 also are novel over the '155 patent. Applicants respectfully request that in light of the above discussion, the rejection of the claims based on the '155 patent be withdrawn and the claims be reconsidered for allowance.

The Examiner further advanced a rejection of claims 1, 19, 24 and 29 under 35 U.S.C. 102(e) as allegedly being anticipated by U.S. Patent 5,869,089 (the '089 patent) which is purported to disclose a transdermal delivery device for treating drug addiction which comprises a drug reservoir containing clonidine and the copolymer of ethylhexyl acrylate and vinyl acetate, a backing of polyester and silicon based release liner. Applicants traverse the rejection.

The '089 patent is directed to programmable transdermal therapeutic systems. While the '089 patent contemplates polyacrylate pressure sensitive adhesives, such adhesives disclosed in '089 are made of butyl acrylate, ethylacrylate, vinyl acetate, 2 methyl acrylic acid and acryl amide ***all together***. This document neither teaches nor suggests a pressure sensitive acrylate-based contact adhesive which consists ***only*** of monomers of 2-ethylhexyl acrylate and vinyl acetate. In the absence of such a teaching, this document does not anticipate the invention of claim 1. Moreover, the '089 patent also does not anticipate the invention of claims 19, 24 and 29 because each of these claims ultimately depend from claim 1.

In light of the above discussions, applicants submit that the claimed invention is novel over the disclosure of both the '155 patent and the '089 patent. Applicants therefore request that the rejection be withdrawn and the claims be reconsidered for allowance.

V. The Rejections Under 35 U.S.C. 103 are Overcome and Should be Overcome.

Claims 1, and 16-29 were rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent 5,965,155 or U.S. Patent 5,869,089, each standing alone or in combination with U.S. Patent 6,024,976 (the '976 patent). Applicants respectfully traverse.

It is well known that in order for a case of *prima facie* obviousness to be properly established, it must be shown that in addition to a requirement for a

teaching of all the claim features, a given combination of references must provide some suggestion or motivation to modify the reference(s) and there must be some reasonable expectation of the success of such modification of the reference. *In re Vaeck*, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). The motivation and the reasonable expectation of success must come from the art and not from the Applicants' own disclosure. As stated in MPEP 2143, all three of the above criteria ***must*** be met in order to properly establish *prima facie* obviousness. It is the Applicants' position that none of these criteria are met by the combination of references cited by the Examiner.

As discussed above neither the '155 patent nor the '089 patent disclose all the elements of the instant invention. More particularly, neither of these documents provide a disclosure of a transdermal delivery system for the delivery of clonidine which system comprises a contact adhesive that consists of a copolymer consisting ***only*** of the monomers of 2-ethlyhexyl acrylate and vinyl acetate. The '976 patent provides no disclosure of a copolymer that is made only of 2-ethylhexyl acrylate and vinyl acetate, indeed, the functional monomers that are used for copolymerization with acrylate monomers of the '976 patent provides no mention that vinyl acetate should be used in the copolymer. The only mention of vinyl acetate in the '976 patent is to be found at column 34, line 33 where vinyl acetate resin is used as a backing material. Hence, it is evident that the documents cited by the Examiner alone and in combination fail to meet the requirement that all the elements of the claimed invention be disclosed.

Moreover, there is no motivation or suggestion to combine the teachings of the '155, or '089 with the teachings of the '976 patent. This motivation to combine must come from the references cited and not from the claimed invention itself. Even if the teachings of the '155 patent, the '089 patent and the '976 patent were fortuitously combined, one of skill in the art would not arrive at the claimed invention. The deficiencies of the '155 and '089 patents are discussed herein above. The '976 patent does nothing to overcome the flaws in the primary references. It merely mentions clonidine in a laundry list of active agents which are combined with a polymer and soluble polyvinyl pyrrolidone. For example, at column 3, line 16-20, provides the '976 patent discloses that "it has been surprisingly found that the use of a soluble PVP results...in the ability to employ higher concentrations of drug

without resulting increased crystallization of the drug." Thus, even if one of skill in the art were to combine the teachings of '976 with those of '089 or '155, that individual would arrive at a transdermal system that required PVP in addition to the other components of the devices of the '155 patent and the '089 patent. The present invention is directed to a simple system in which the copolymer is comprised only of the monomers of 2-ethylhexyl acrylate and vinyl acetate, without the need for additional membranes, monomers or PVP. Such a simple system is not suggested or taught by the documents cited by the Examiner.

Moreover, the instant invention concerns a transdermal system which does not use a membrane controlling the release of the active agent as is required by the '155 patent but instead provides a matrix system that is made up of only the monomers of 2-ethylhexyl acrylate and vinyl acetate. In view of the fact that the '089 system uses a system that requires a release rate controlling membrane and a polyacrylate consisting of 5 monomers, there would have been no expectation that eliminating the rate controlling membrane and 3 components of the polymer of the '089 patent would successfully yield a system that would provide a transdermal delivery of clonidine.

In summary, Applicants submit that the cited references, either alone or in combination, fail to teach or suggest all the elements of claim 1; there is no motivation or suggestion to combine the teachings of the cited references and even if one of skill in the art were to combine the references, there would be no expectation of success of achieving the claimed invention. The references do not establish the alleged *prima facie* obviousness of the invention of Claim 1. Claims 16-29 ultimately depend from Claim 1 and are thus also are patentably non-obvious over the cited references. In view of the foregoing, Applicants respectfully request that the rejections of Claims 1 and 16-29 under 35 U.S.C. §103(a) over '089 or '155 in view of '976 be withdrawn and the claims be reconsidered for allowance.

VI. Conclusion

Applicants believe all the claims are now in a condition for allowance. Favorable reconsideration of the application is respectfully requested. The Examiner is invited to contact the undersigned with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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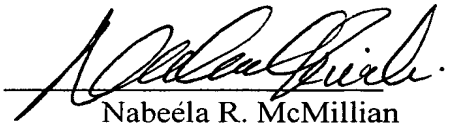
June 18, 2001 By: 

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APPENDIX A
MARKED UP VERSION OF AMENDMENTS MADE HEREIN

In the Claims:

1. (Amended) A transdermal system for the delivery of clonidine consisting of a clonidine-containing pressure-sensitive acrylate-based contact adhesive layer consisting of a copolymer consisting of the monomers 2-ethylhexyl acrylate and vinyl acetate; a covering and, on a side opposite from the covering, a removable support that temporarily covers the contact adhesive layer.

25. (Amended) The transdermal system of claim 19 wherein the [dry] contact adhesive layer has a dry weight per unit area of from 20 g/m^2 to 150 g/m^2

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